REMARKS

The Office Action dated May 14, 2008 has been received and carefully studied.

A Request for Continued Examination is filed herewith.

The Examiner rejects claim 15 under 35 U.S.C. §103(a) as being unpatentable over Altomare et al., J. Med. Chem., 1998, pp. 3812-3820, over Nagarajan et al., J. Med. Chem., 1976, pp. 508-511; and Petrie et al., U.S. Patent No. 5,919,808. The Examiner states that the claimed compounds are homologs and/or position isomers of the reference compounds, and considers that a prima facie case of obviousness has been established as a result of the close structural similarity of the compounds.

By the accompanying amendment, claims 1-7, 9, 10, 12 and 16-25 have been cancelled without prejudice.

Also by the accompanying amendment, claim 15 has been amended by deleting therefrom the 3-phenyl-cinnoline compound of the formula (2), and by eliminating from the definition of X a lower alkoxyl group having 1 to 6 carbon atoms. The compound of the formula (1) is fully supported by the synthesis data in the Examples and pharmacological data in the Test Examples of the specification.

The compound of the formula (1) as recited in claim 15 as amended is characterized in that the compound has a substituted 3-phenylpyridazine structure in the molecule and has an effective antitumor activity. Indeed, Test Examples 1 and 2 demonstrate that the compound of the formula (1) has a proliferation inhibition activity on mammary cell such as MCF-7, MDA-MB-453 and ZR-75-1.

Altomare et al. describe condensed pyridazines of formulae 28 and 29 at page 3813, column 2. However, the compounds of Altomare et al. have an unsubstituted 3-phenylpyridazine structure in the molecule, whereas the claimed compounds of the present invention have a substituted 3-phenylpyridazine structure in the molecule.

Furthermore, the compounds of Altomare et al. have an inhibition activity on monoamine oxidase-B and are useful in the treatment of Alzheimer's diseases, whereas the claimed compounds of the present invention have an antitumor activity and are useful in the treatment of tumor.

Thus, the claimed compounds are evidently different from that of Altomare et al. in chemical structure and pharmacological activity, and Altomare et al. fail to teach or suggest the claimed compounds and their pharmacological activity.

To further support the distinct difference between the claimed compounds and Altomare et al., additional tests were carried out in the same way as those of Test Example 1 of the specification to generate comparative pharmacological data. Thus, the compound of Example 66 of the specification was compared to Compounds A and B shown in the accompanying Declaration in Table 1 in inhibition activity on mammary cells such as MCF-7 and MDA-MB-453. Compound A has an unsubstituted 3-phenylpyridazine structure in the molecule, similar to the compounds of formulae 28 and 29 of Altomare et al. Compound B has no substituent at the 5-position in the molecule, similar to the compound of formula 26 of Altomare et al.

As can be seen from the results of Table 1, the inhibition activities of Compounds A and B on mammary tumor cell are less potent than that of the compound of Example 66 of the specification.

The results indicate that Compounds A and B, which are similar to the compounds 29, 28 and 26 of Altomare et al. in chemical structure, have less potent inhibition activity on mammary tumor cell than the compound of Example 66 of the specification. That is, the results show that the substituted 3-phenylpyridazine structure and the substituent

at the 5-position, which the claimed compounds of the present invention have, are required for high inhibition activity on mammary tumor cell.

It is noted that Table 2 of the present specification provides additional data for Compounds of Examples 1, 2, 6, 9, 10, 11, 13, 20, 24, 26, 27, 70, 71, 72 and 73 within the scope of amended claim 1, except for the Compound of Example 65. These data in Table 2 show that various compounds within the scope of amended claim 1 have a higher inhibition activity on mammary cells than Compounds A and B in Table 1 of the Declaration.

Altomare et al. neither teach nor suggest that the substituted 3-phenylpyridazine structure and the substituent at the 5-position, which the claimed compounds of the present invention have, are required for high inhibition activity on mammary tumor cell.

Consequently, Altomare et al. fail to teach or suggest the claimed compounds of the present invention and the pharmacological effects thereof.

Nagarajan describes a 5-oxo-1,4,5,6,7,8-hexahydrocinnoline of compound No. 14 in Table 1, on page 509. Thus, Nagarajan describes the compound having an unsubstituted 3-phenyldihydropyridazine structure in the

molecule. Therefore, the compound of Nagarajan is evidently different from the claimed compounds in chemical structure, as the claimed compounds have a substituted 3-phenylpyridazine structure, which is a plane stereo structure, whereas the compound of Nagarajan does not have a plane stereo structure.

Furthermore, the compound of Nagarajan has central nervous system activity, and is useful as an antidepressant, whereas the claimed compounds of the present invention have an antitumor activity and are useful as an antitumor medicine.

Consequently, Nagarajan fails to teach or suggest the claimed compounds of the present invention and the pharmacological effects thereof.

Petrie describes substituted 3-phenyldihydropyridazine 7,7-dimethyl compounds (No. 92-8215 and No. 92-8372) in FIG. 4B and FIG. 4C. Thus, Petrie describes the compound having a substituted 3-phenyldihydropyridazine structure, which is not a plane stereo structure and which is different from the substituted 3-phenylpyridazine structure of the claimed compounds of the present invention.

Furthermore, the compounds of Petrie are useful in the treatment of bone deficit conditions.

Consequently, Petrie fails to teach of suggest the claimed compounds of the present invention and the pharmacological effects thereof.

Reconsideration and allowance is respectfully requested in view of the foregoing.

Respectfully submitted,

Kevin S. Lemack
Reg. No. 32,579
176 E. Main Street - Suite 5
Westboro, Massachusetts 01581
Tel: (508) 898-1818

Appendix

A Rule 132 Declaration is attached hereto.